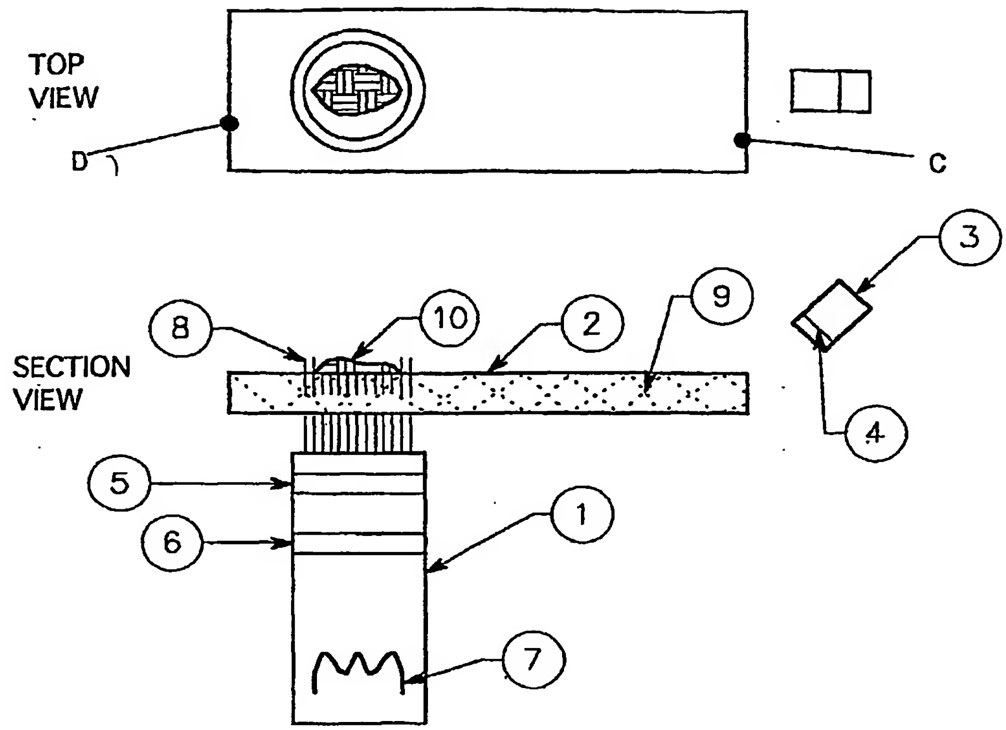


No.	Key	Function
1	Light Source	Provides photo excitation
2	Planar Wave Guide (PWG)	Sample substrate & carrier for emission light
3	Photo Detector	Detects light emitted from sample
4	Emission Filter	Filter that allows only emission wave length to pass
5	Optics	Collimates light emitted from lamp
6	Excitation Filter	Filter that allows only excitation wave length to pass
7	Lamp	Produces light
8	Excitation Rays	
9	Emission Rays	
10	Probe Surface	Target Hybridization for later detection

Figure 1

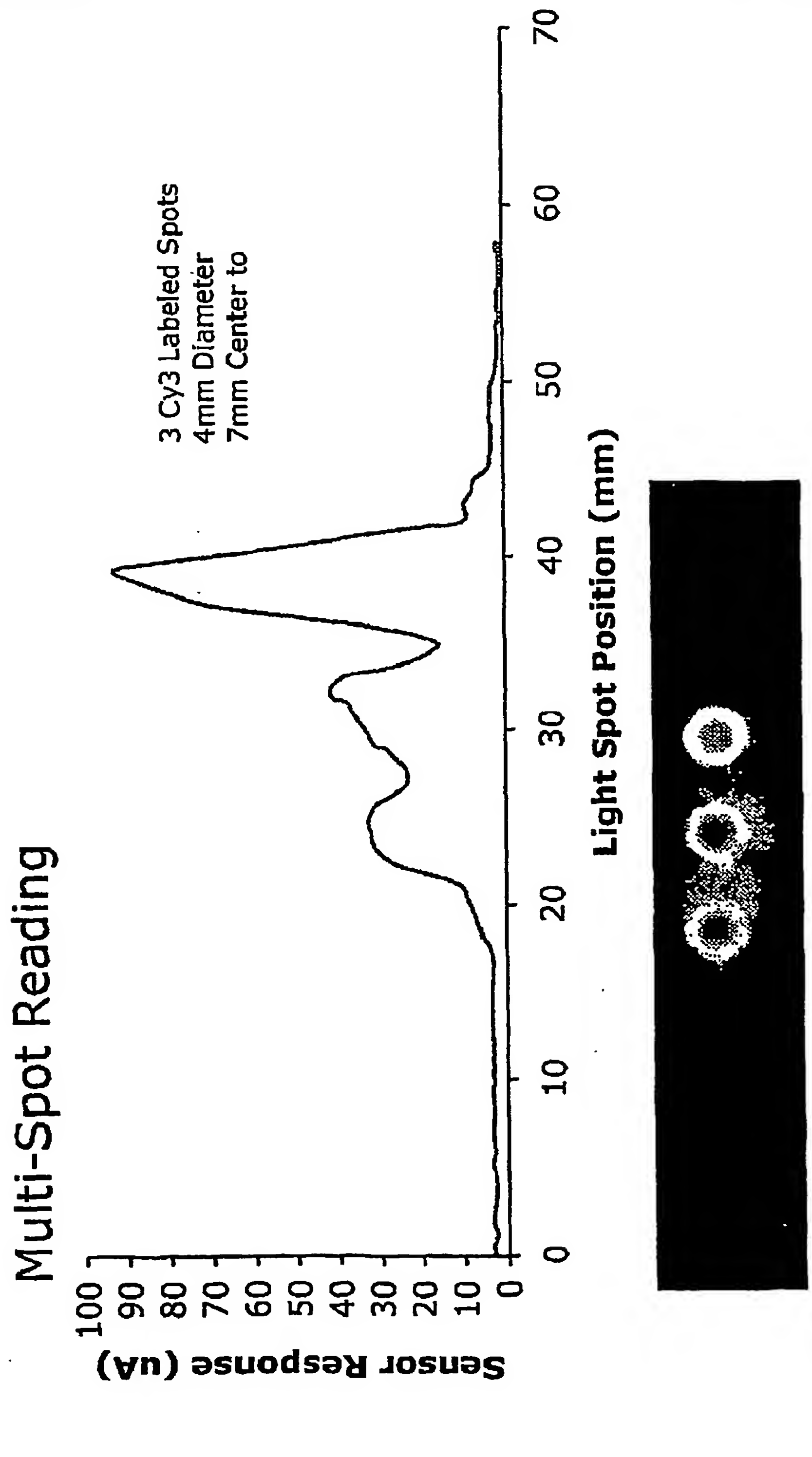
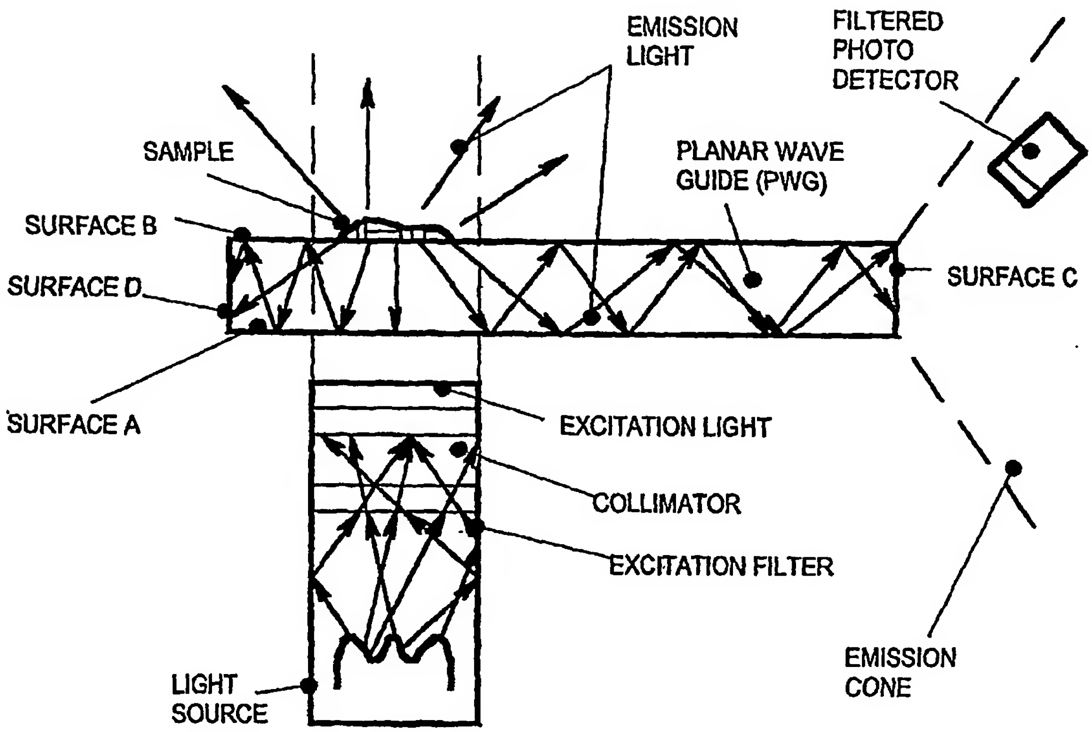
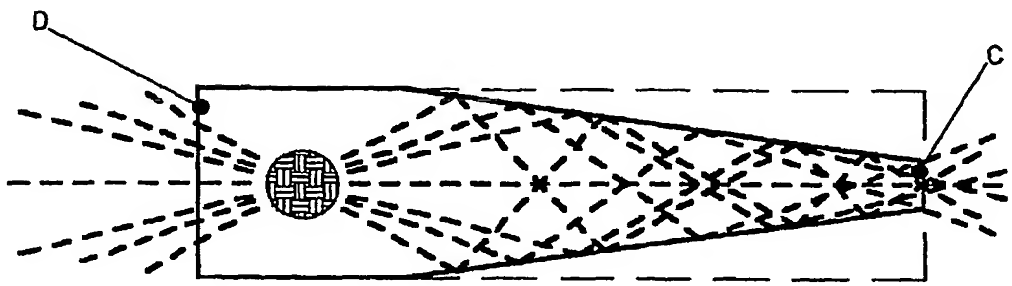

Multi-Spot Reading
3 Cy3 Labeled Spots
4mm Diameter
7mm Center to
Sensor Response (uA)
100
90
80
70
60
50
40
30
20
10
0
0
10
20
30
40
50
60
70
Light Spot Position (mm)

Figure 2



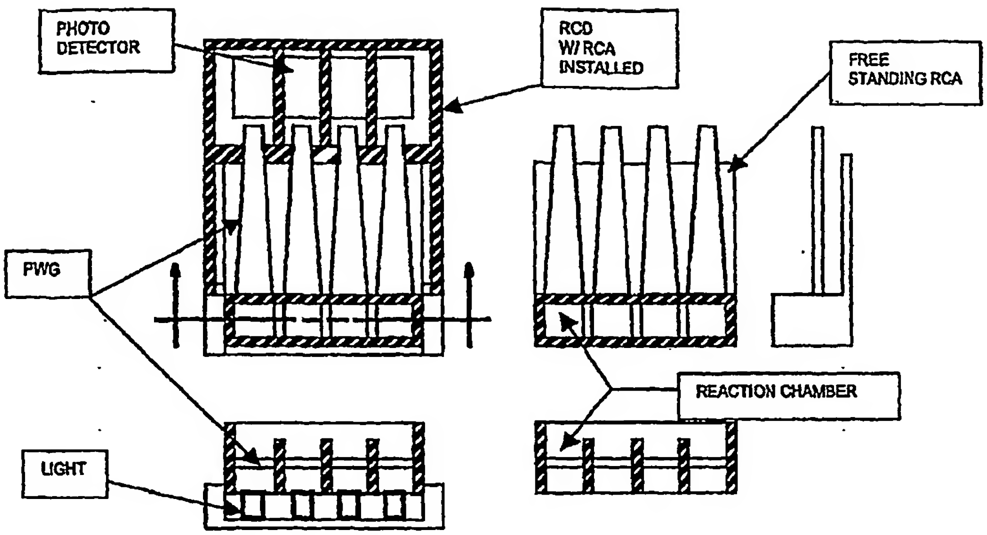
Light Path Illustration

Figure 3



Focusing PWG

Figure 4



Multiplexing Means 1 Illustration

Figure 5

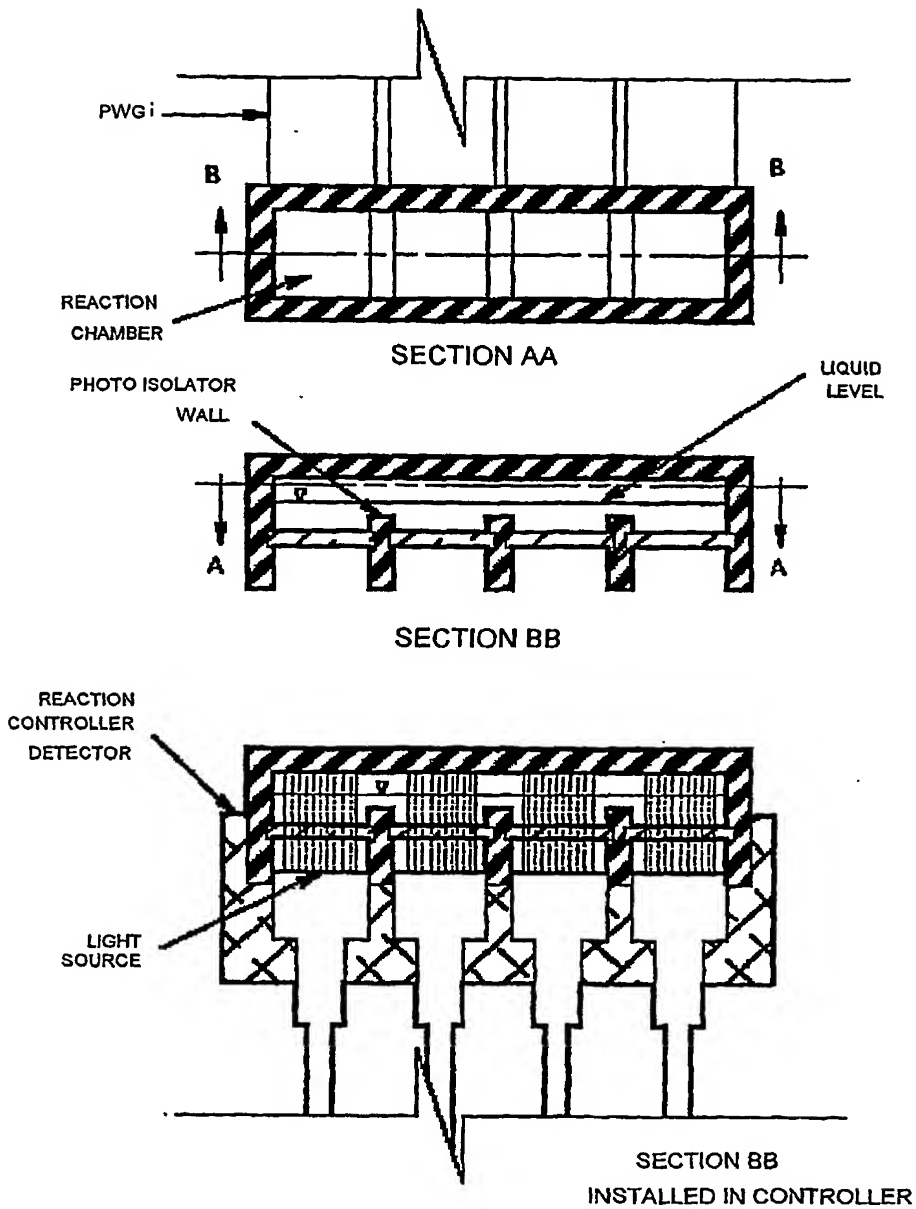
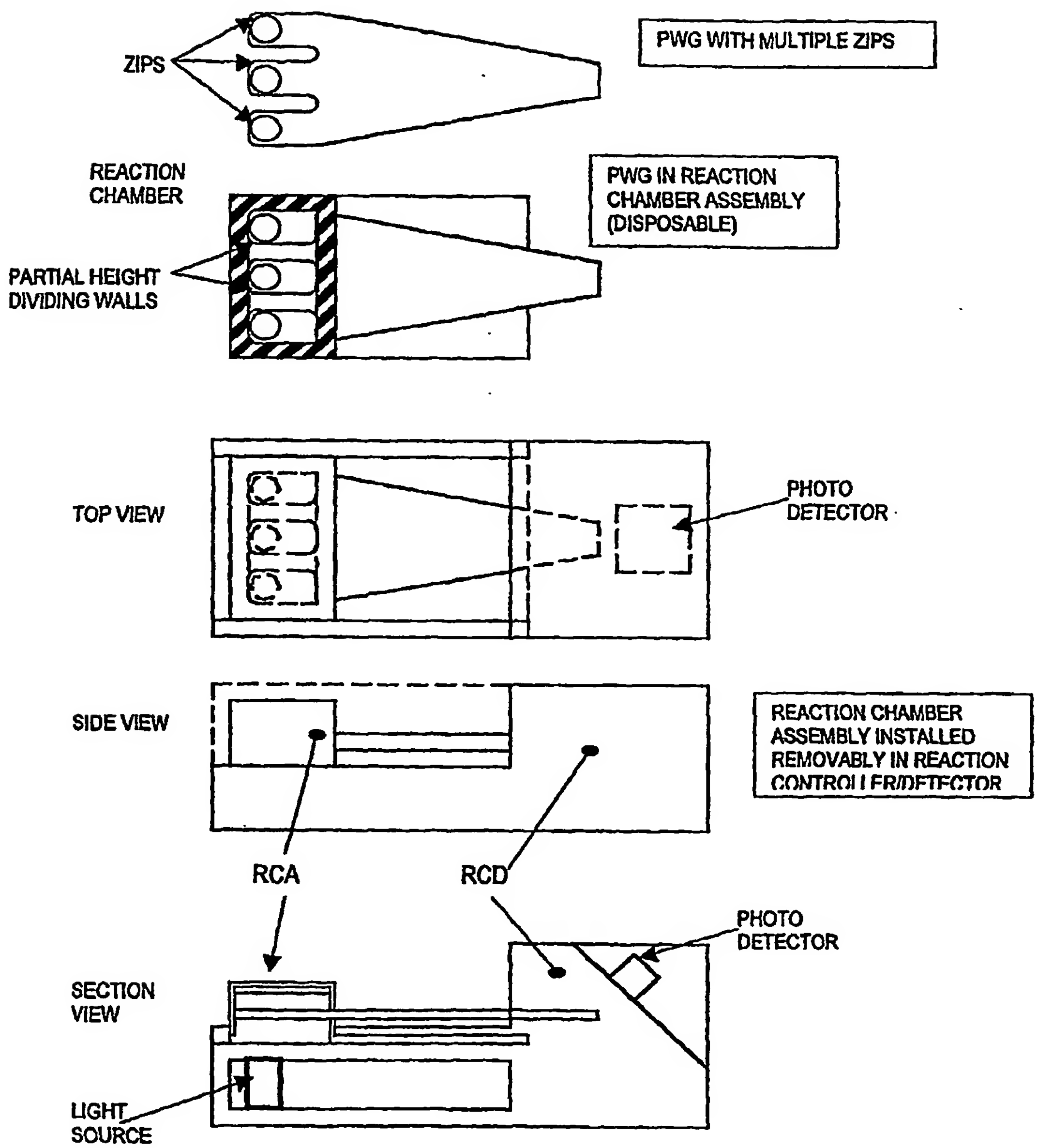


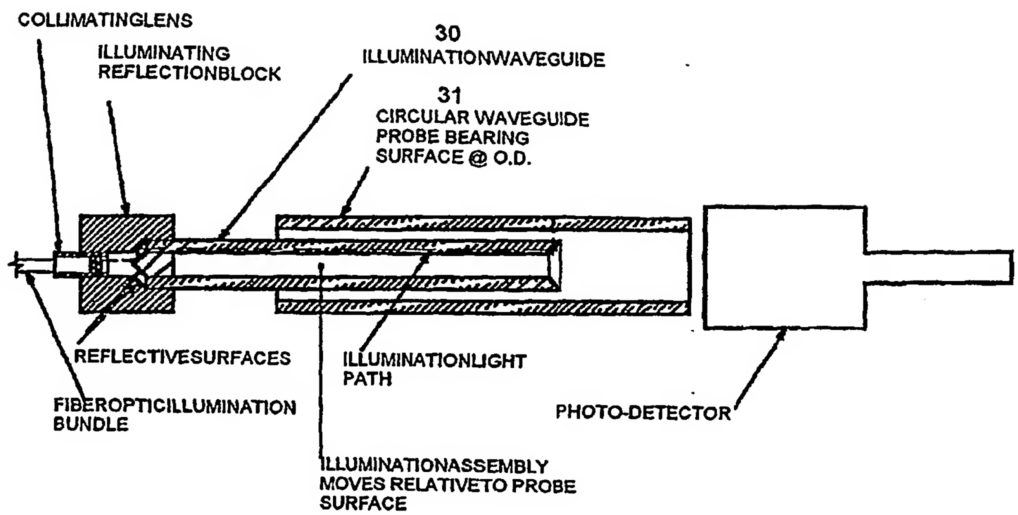
Photo Isolation Illustration

Figure 6



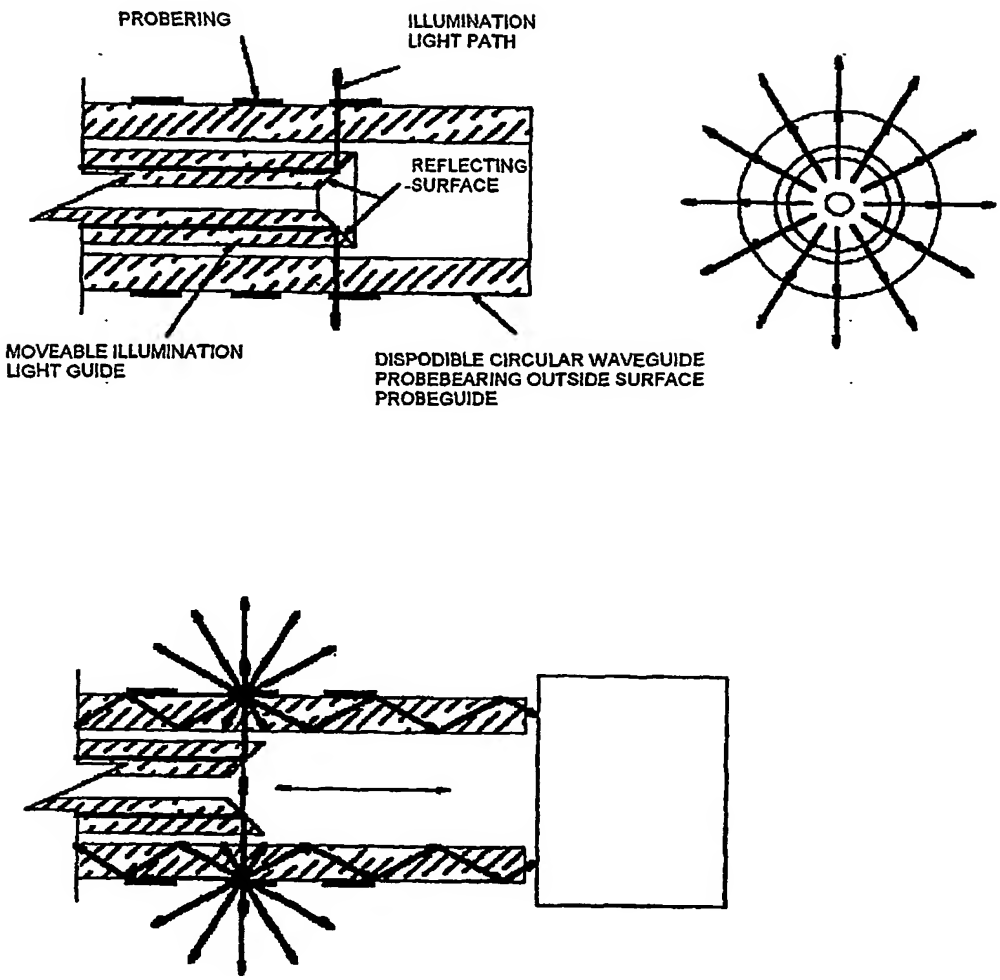
Multiplexing Means

Figure 7



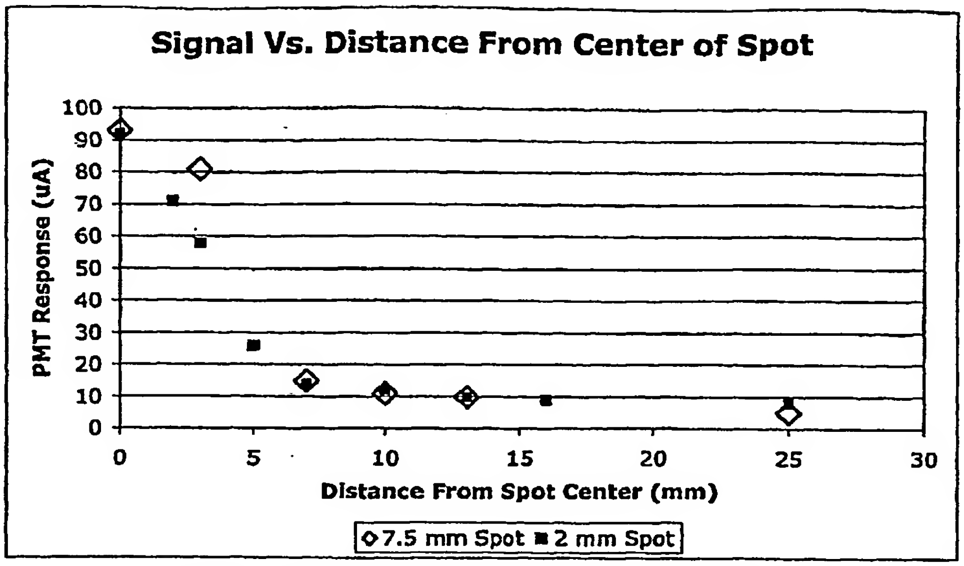
Tubular CWG Detection

Figure 8



Tubular CWG Distal End

Figure 9



Emission Decay Data Vs. Excitation Light Alignment

Figure 10

Figure 11a

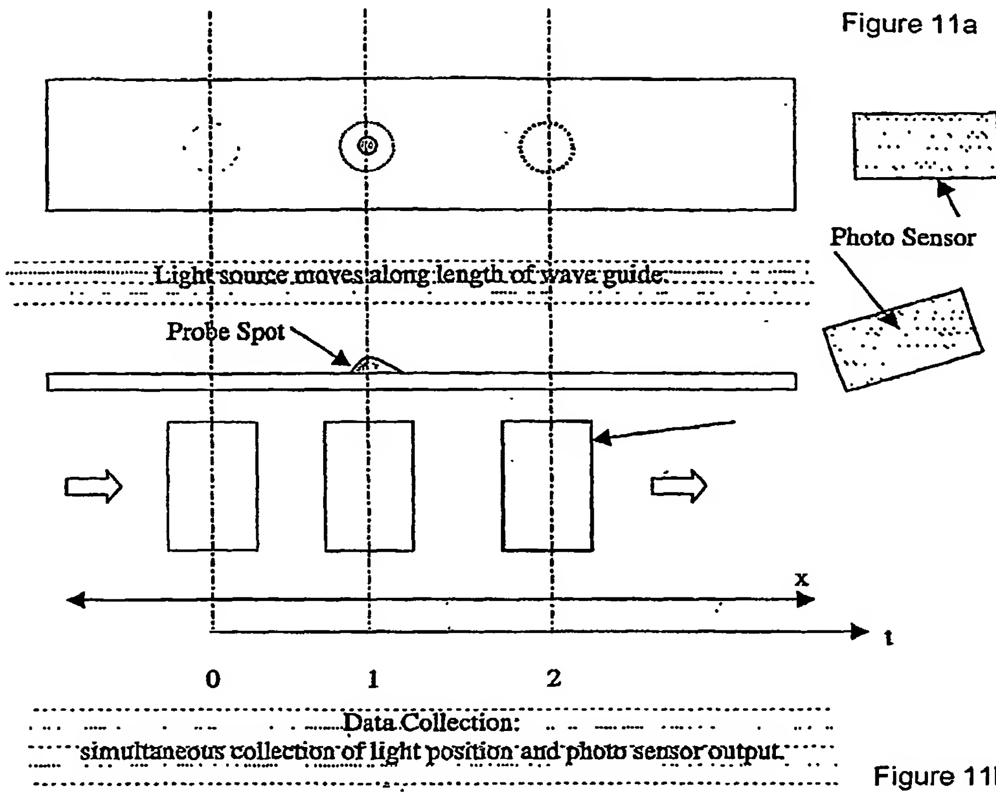
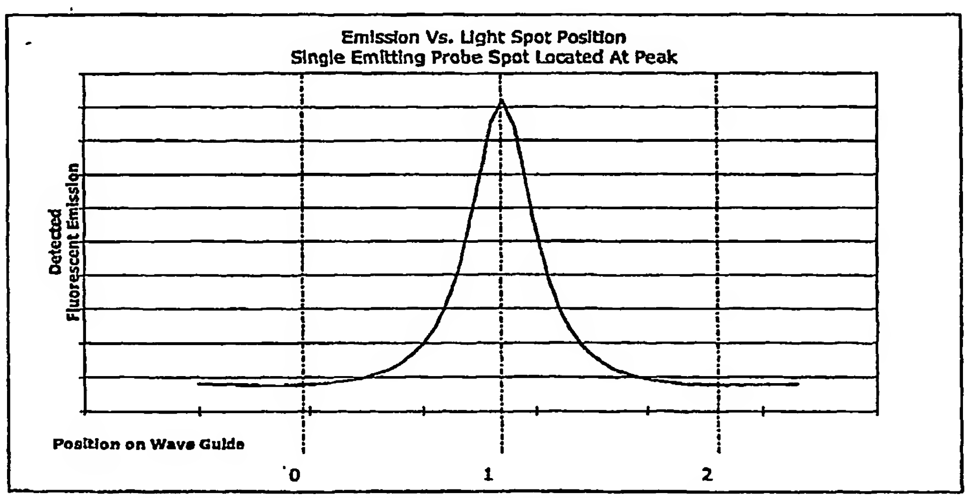
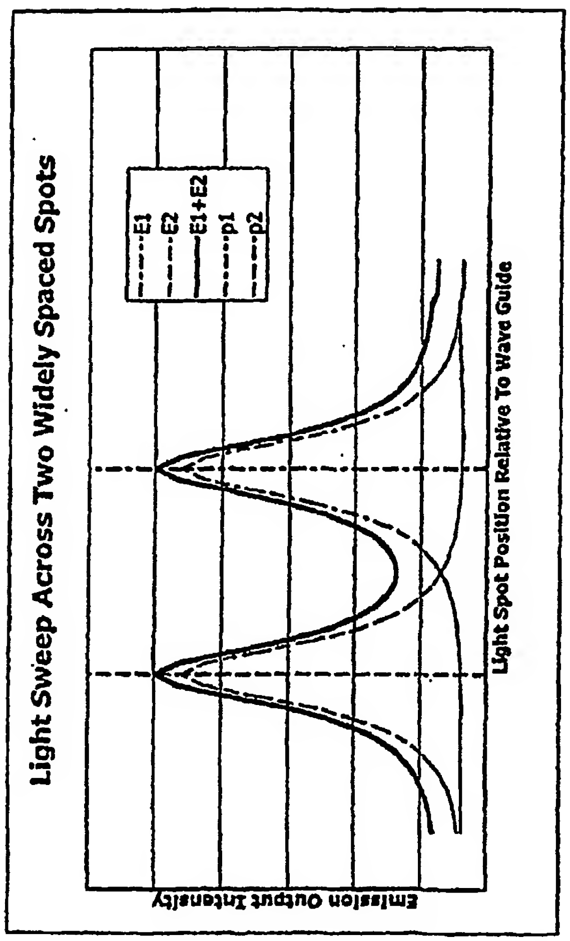


Figure 11b

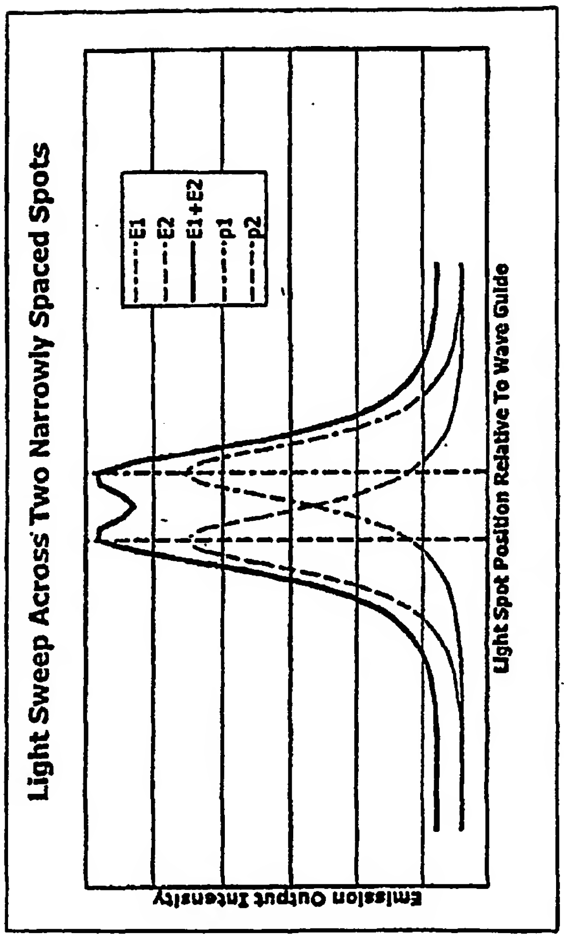


Data Collection Method & Projected Readings



Two Spot Sweep Data, Wide Spacing

Figure 12



Two Spot Sweep Data, Narrow Spacing

Figure 13

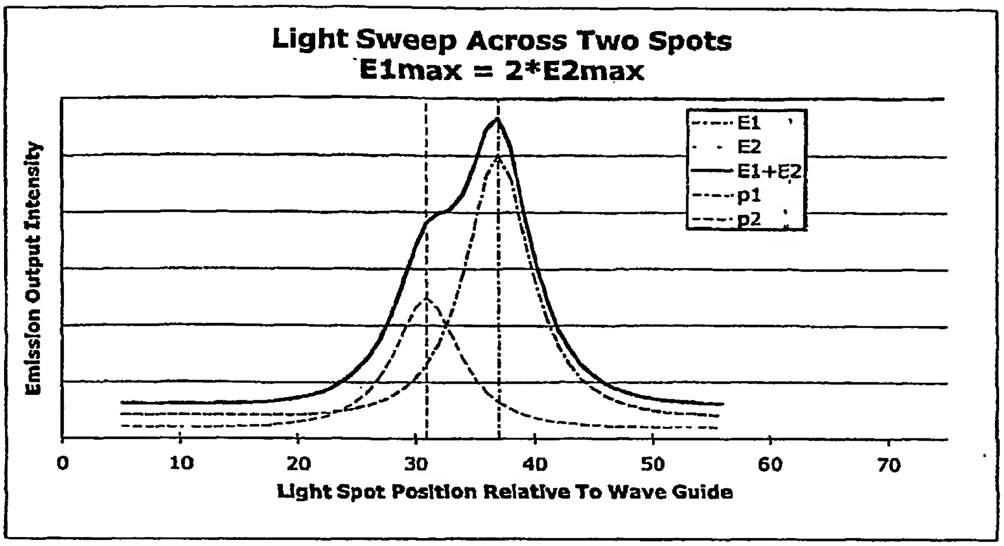

Light Sweep Across Two Spots
E1max = 2*E2max
E1
E2
E1+E2
p1
p2
Emission Output Intensity
0
10
20
30
40
50
60
70
Light Spot Position Relative To Wave Guide

Figure 14

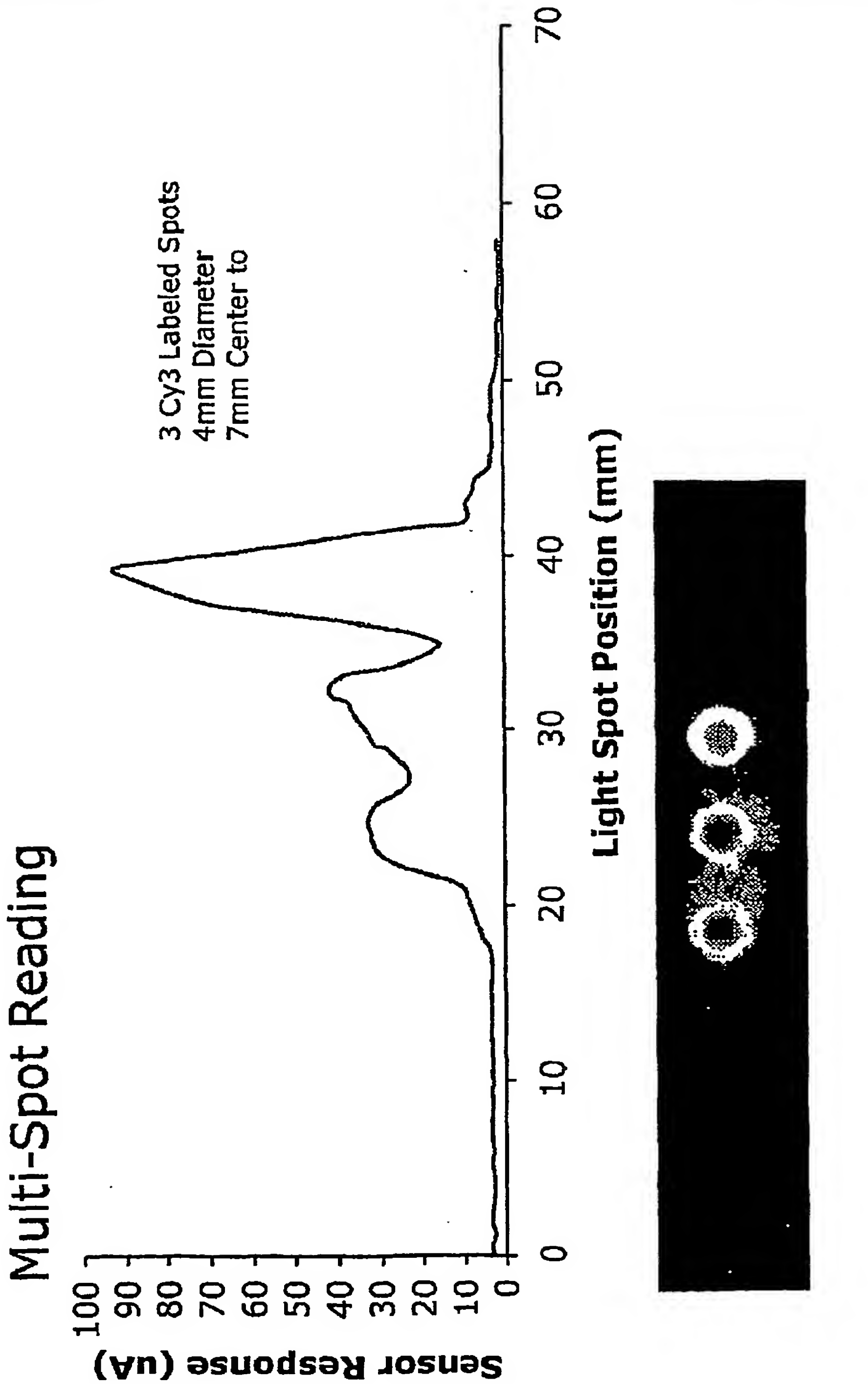

Multi-Spot Reading
3 Cy3 Labeled Spots
4mm Diameter
7mm Center to
Sensor Response (uA)
100 90 80 70 60 50 40 30 20 10 0
0 10 20 30 40 50 60 70
Light Spot Position (mm)

Figure 15

$$E = \sum_{i=1}^{n} E_i \tag{1}$$

E: Total fluorescent emission output associated with a given excitation light spot location.

E_i: Fluorescent emission generated from a fluorescent spot *i*.

Assumption 3 is based on empirical data that has been collected showing that such a relationship does exist. The derived relation, in its basic form is shown in equations 2 and 3.

$$E_i = E_{\max,i}\left\{1-\left[\frac{(x_s-x_i)^2}{\beta+(x_s-x_i)^2}\right]+\left[\frac{abs\,(x_s-x_i)}{\alpha+abs\,(x_s-x_i)}\right]\right\}+Z \tag{2}$$

$$E_i = E_{\max,i}(A_{s,i})+Z \tag{3}$$

x_s: Position of excitation light source relative to waveguide surface coordinates.

x_i: Position of fluorescent source location *i*.

E_{max}: Maximum fluorescent emission from source *i*. This emission occurs where $x_s = x_i$.

β, α: Constants determined by dimensional parameters of slide, excitation light spot, and fluorescent source.

Z: Background fluorescence measured.

This expression was derived from data taken of single spots hybridized to a slide (waveguide) surface.

Deconvolution Method

The actual mathematical method of deconvolution recognizes through assumptions 1, 2, and 3, that individual maxima of emission from each of the possible fluorescent sources can be determined by simultaneously solving a series of linear equations. The number of equations is equal to the number of unknown fluorescent source values that are sought. Following basic rules of linear algebra, the linear equations can be solved following the general expressions in Equation 4.

$$\begin{gathered}[A]\{E_{max}\}=\{E\}-Z\\ \{E_{max}\}=[A]^{-1}\{E\}-Z\end{gathered} \tag{4}$$

Figure 16

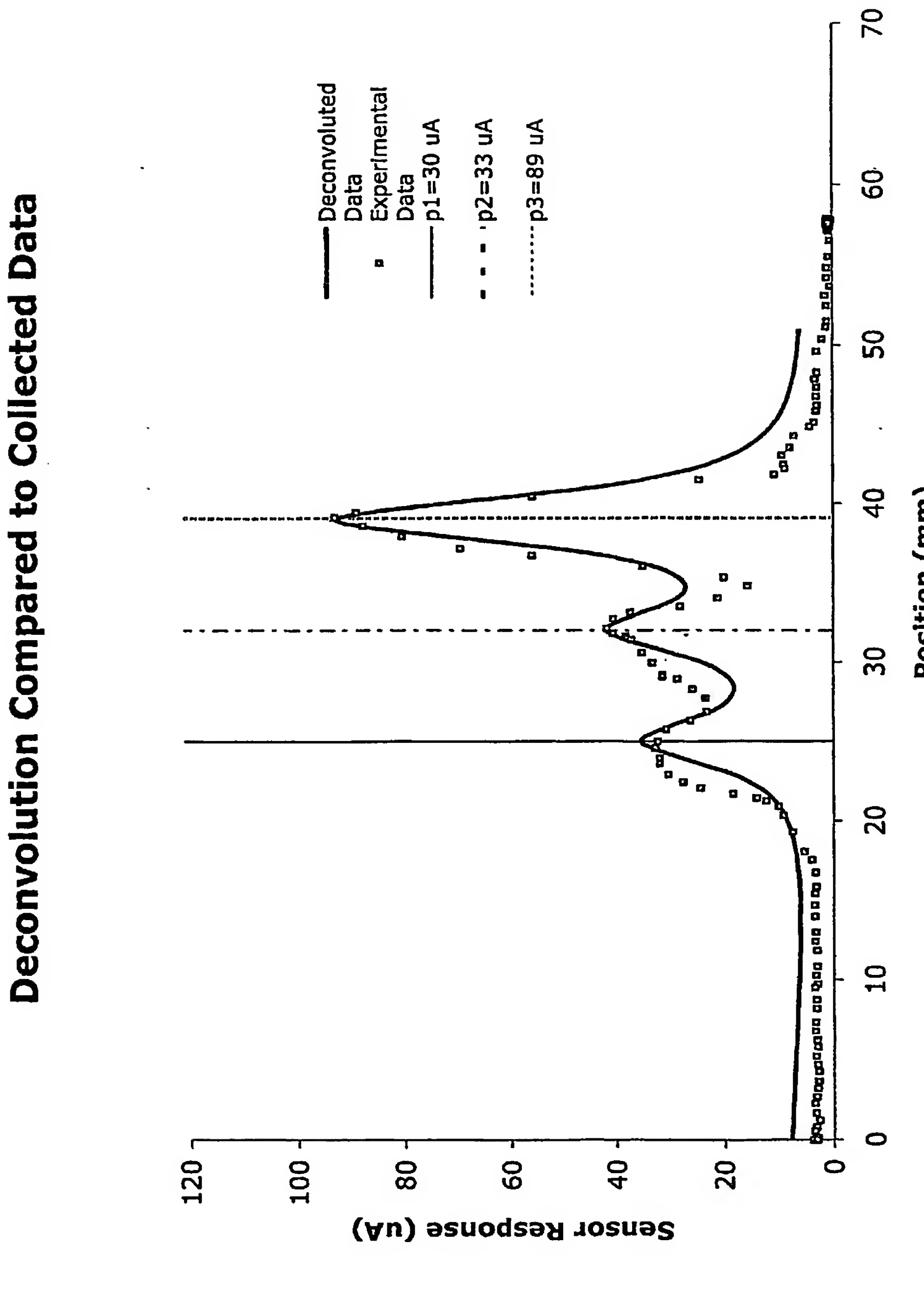


Figure 17

SUBSTITUTE SHEET (RULE 26)

$$E_\gamma = \sum_{\gamma=1}^{n} E_{\gamma,\varphi} + Z \qquad (1)$$

E_γ: Total fluorescent emission output associated with a given excitation light spot location.

$E_{\gamma,\phi}$: Fluorescent emission generated from source ϕ.

$$E_{\gamma,\varphi} = E_{\max\varphi}\left\{1-\left[\frac{r_{\gamma,\varphi}{}^2}{\beta+r_{\gamma,\varphi}{}^2}\right]+\left[\frac{r_{\gamma,\varphi}}{\alpha+r_{\gamma,\varphi}}\right]\right\} \qquad (2)\ \{\text{Developed from empirical observations}\}$$

$$E_{\gamma,\varphi} = E_{\max,\varphi}(A_{\varphi,\gamma}) + Z \qquad (3)$$

$r_{\gamma,\phi}$: Distance between fluorescent source, ϕ, and light spot γ.

$E_{\max,\phi}$:Maximum fluorescent emission from source ϕ @ $r_{\gamma,\phi}=0$.

β,α: Constants determined by dimensional parameters of slide, excitation light spot, and fluorescent source.

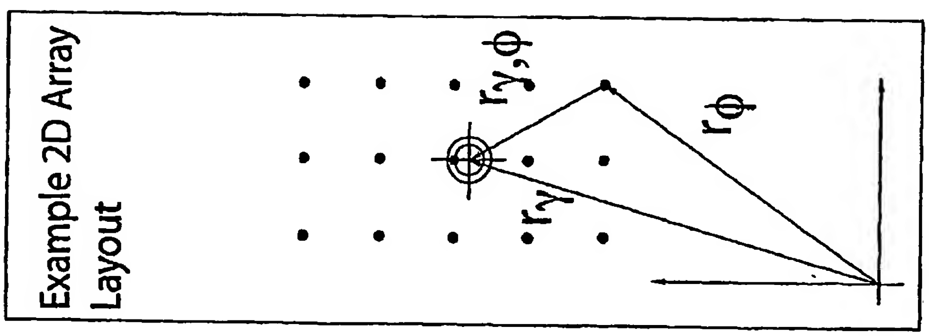
Z: Background fluorescence measured.

$$\begin{aligned}[A]\{E_{\max}\} &= \{E\} - Z \\ \{E_{\max}\} &= [A]^{-1}\{E\} - Z\end{aligned} \qquad (4)$$

The distance $r_{\gamma,\phi}$ as defined is derived from the vectors $\mathbf{r}_\gamma$ and $\mathbf{r}_\phi$ as shown in Figure 19. The origin of the system shown in Figure 19 is predefined relative to the array. The method prescribes, through these assumptions and definitions, simultaneously solving a series of equations whose number is equal to that of the unknown loci (Equation 4). The product of deconvolution, $\{E_{\max}\}$, is the vector of individual and independent maxima of fluorescent emission from each potential source in the array.

Figure 18

Figure 19



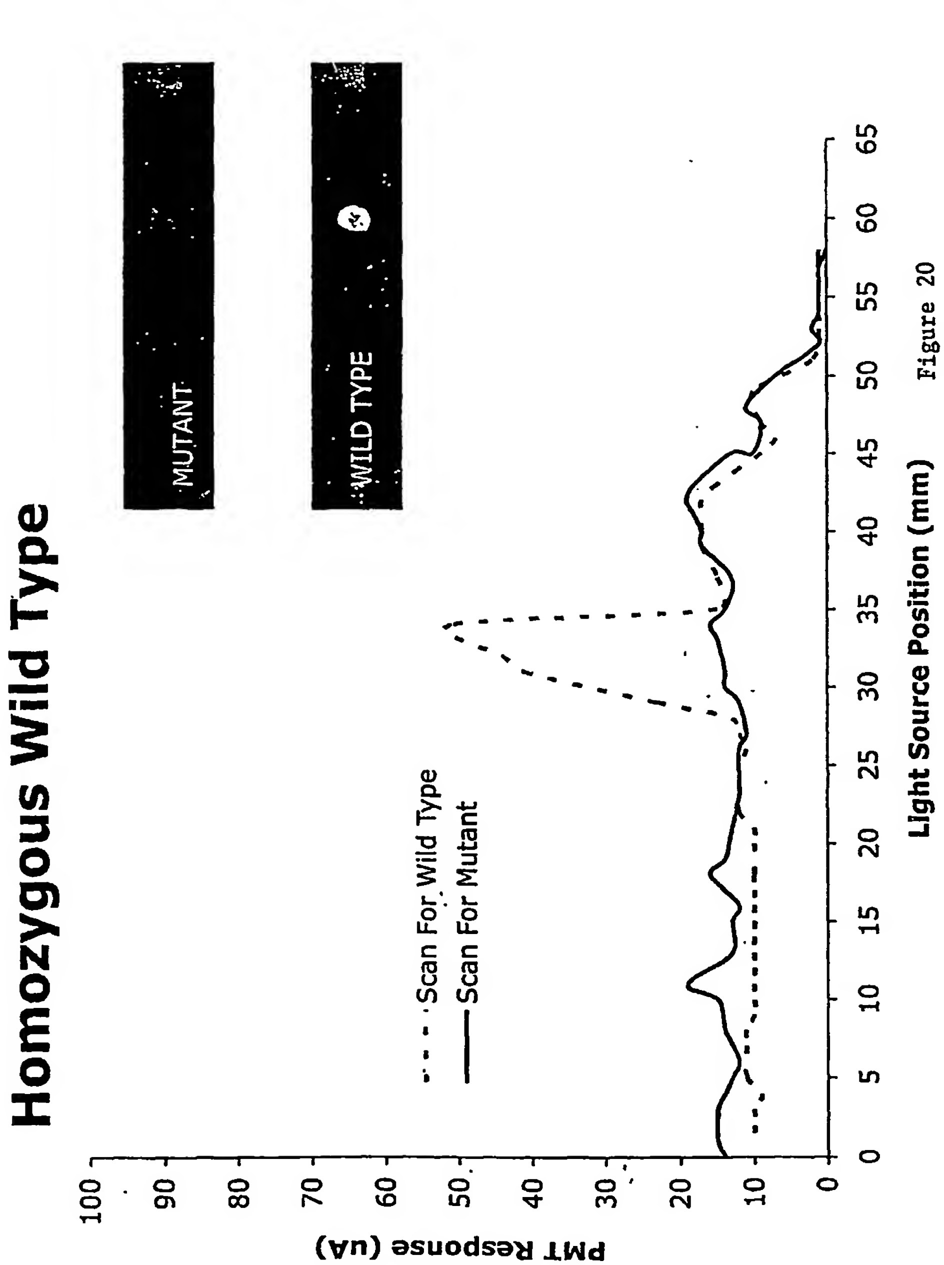

Homozygous Wild Type
MUTANT
WILD TYPE
Scan For Wild Type
Scan For Mutant
PMT Response (uA)
100
90
80
70
60
50
40
30
20
10
0
0
5
10
15
20
25
30
35
40
45
50
55
60
65
Light Source Position (mm)

Figure 20

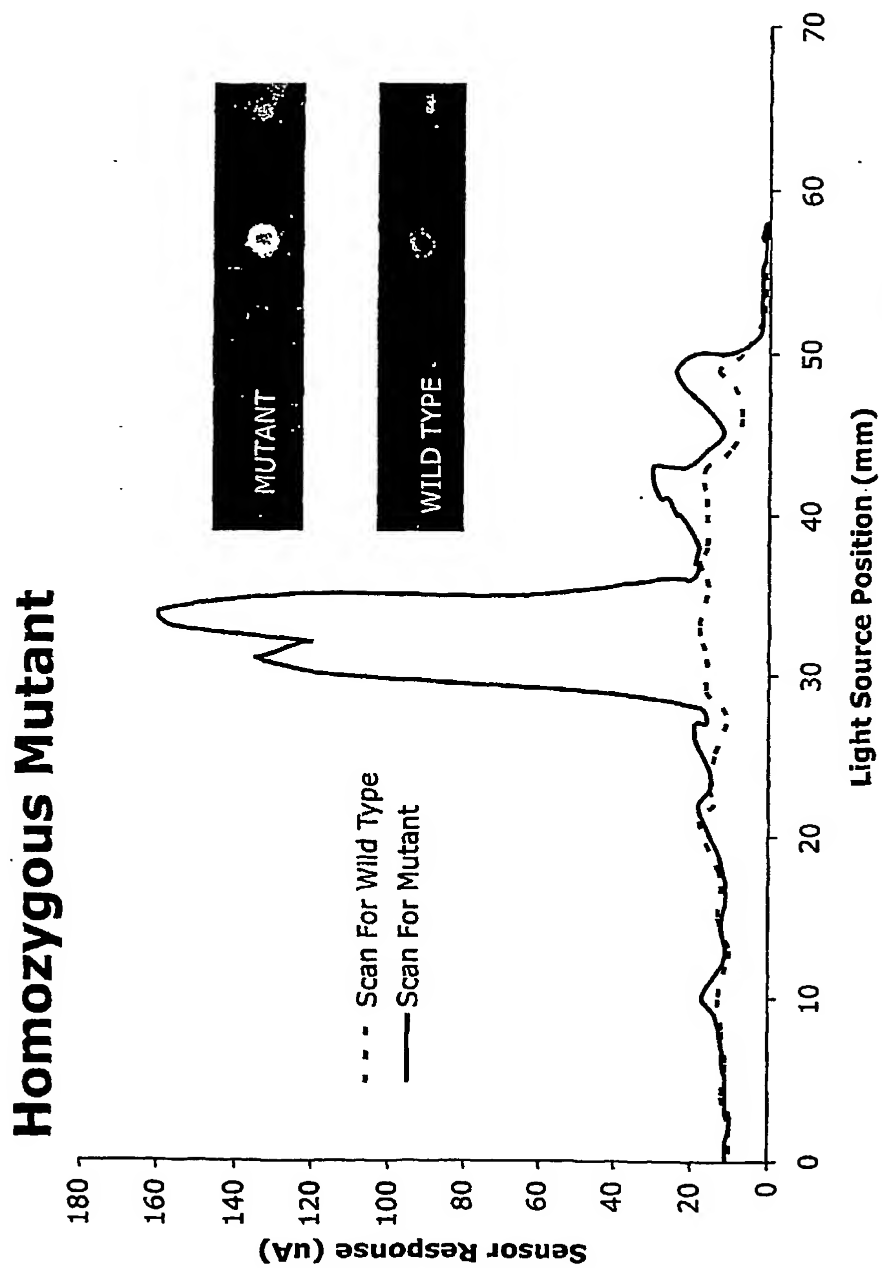

Homozygous Mutant
Scan For Wild Type
Scan For Mutant
MUTANT
WILD TYPE
Sensor Response (uA)
180
160
140
120
100
80
60
40
20
0
Light Source Position (mm)
0
10
20
30
40
50
60
70

Figure 21

Spec. No.	Clinical Wild Type	Clinical Mutant	Laser Scanner Wild Type	Laser Scanner Mutant	PWG Device Wild Type	PWG Device Mutant
1	+	-	+	-	+	-
2	+	-	+	-	[redacted]	-
3	+	-	+	-	+	-
4	+	-	+	-	+	-
5	+	-	+	-	+	-
6	+	-	+	-	+	-
7	+	-	+	-	+	-
8	+	-	+	-	+	-
9	+	-	+	-	+	-
10	+	-	+	-	+	-
11	+	-	+	-	+	-
12	+	-	+	-	+	-
13	+	-	+	-	+	-
14	+	-	+	-	+	-
15	+	-	+	-	+	-
16	+	-	+	-	+	-
17	+	-	+	-	+	-
18	-	+	-	+	-	+
19	-	+	-	+	-	+
20	-	+	-	+	-	+
21	-	+	-	+	-	+

Figure 22

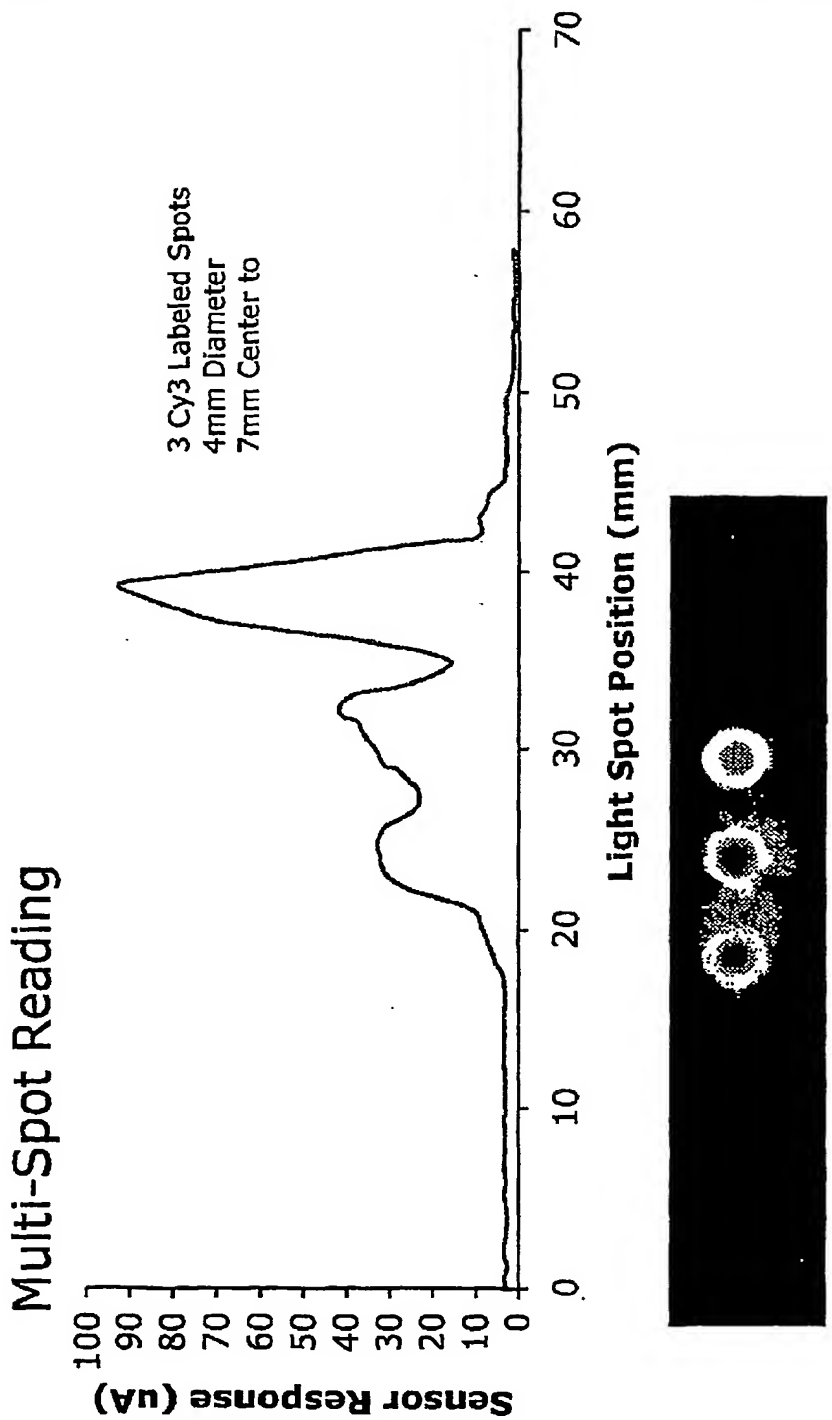

Multi-Spot Reading
Sensor Response (uA)
100 90 80 70 60 50 40 30 20 10 0
0 10 20 30 40 50 60 70
Light Spot Position (mm)
3 Cy3 Labeled Spots
4mm Diameter
7mm Center to

Figure 23

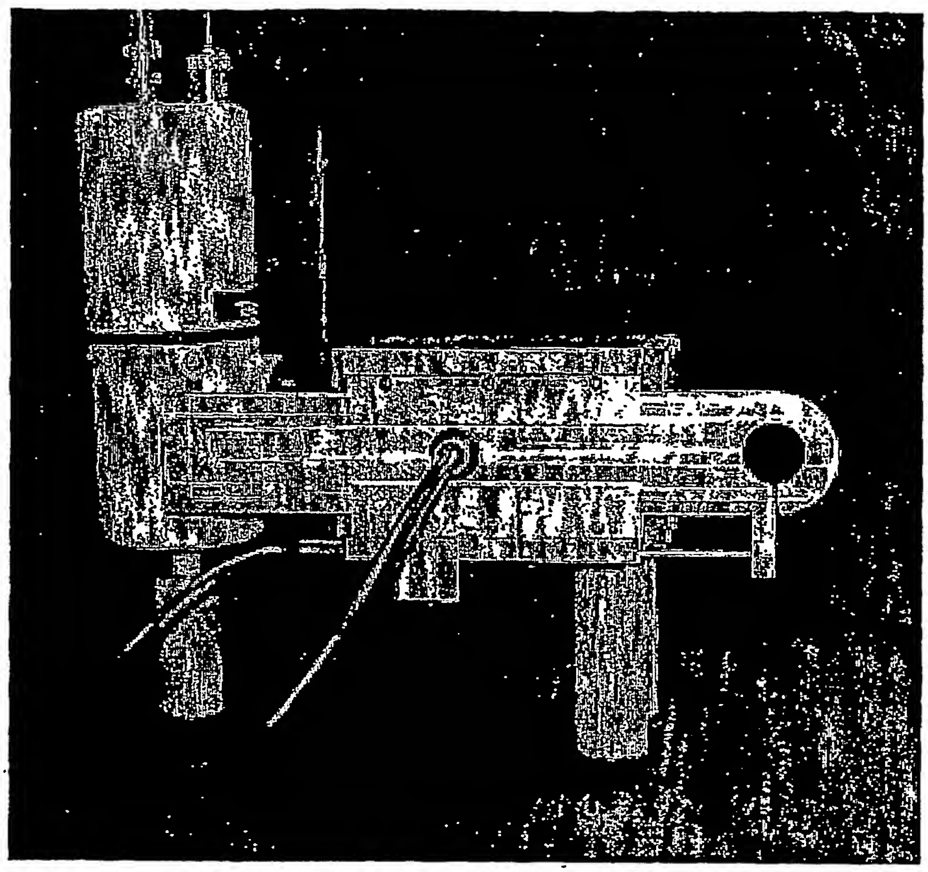


Figure 24

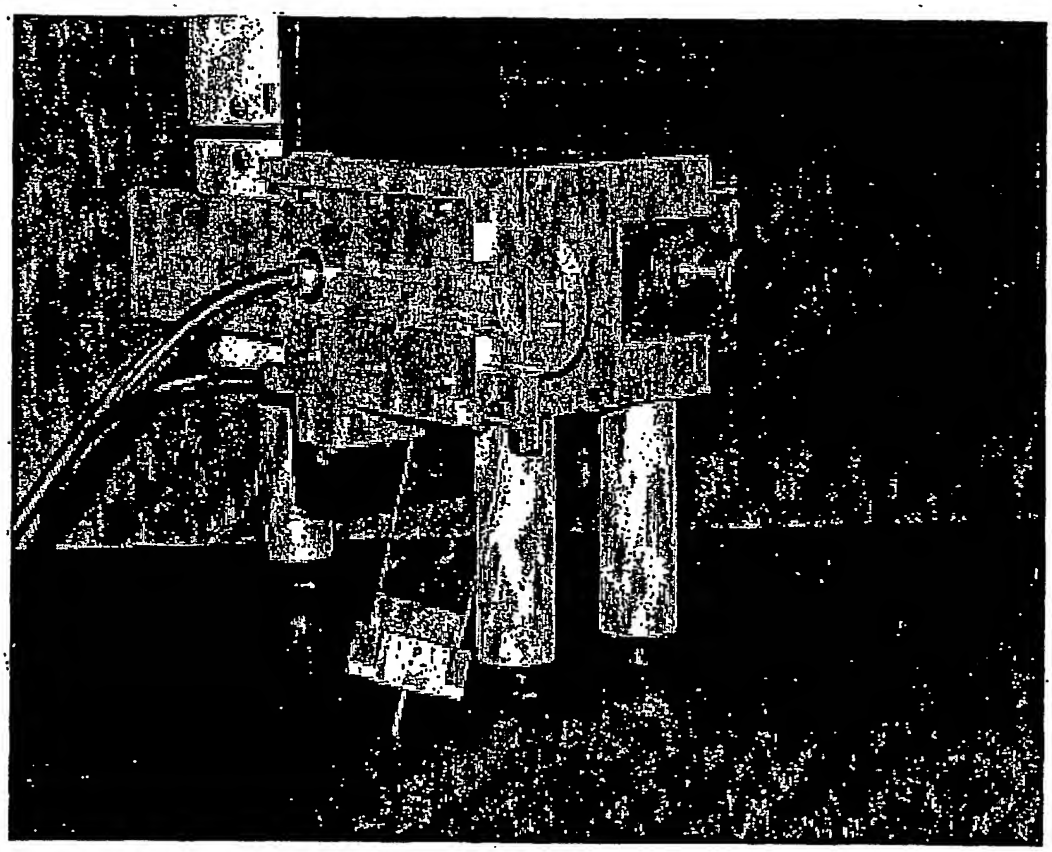
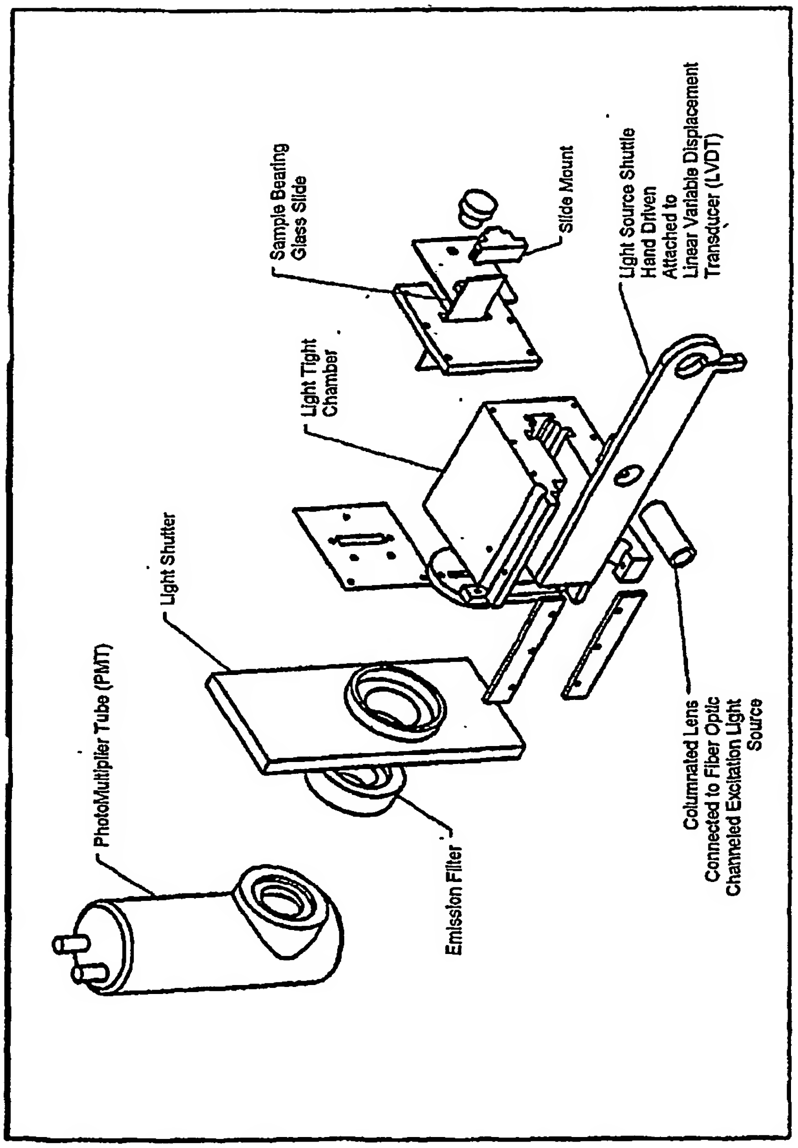


Figure 25



An Exploded Diagram of the System Depicted in the Photograph in Figure 25.

Figure 26